



PATENT

Docket No. DIV-1460-21US (112766-199)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Short et al. Confirmation No. 4125
U.S. Serial No.: 10/029,221
Filing Date: December 21, 2001
Title: EXONUCLEASE-MEDIATED NUCLEIC ACID REASSEMBLY IN
DIRECTED EVOLUTIONS

Hand Carried directly to Customer Window at:
2011 South Clark Place
Crystal Plaza Two, Lobby, Room 1B03, Box Sequence
Arlington, VA 22202

**COMMUNICATION IN REPLY TO NOVEMBER 29, 2002 NOTICE TO COMPLY WITH
REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE
SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

Dear Commissioner:

This Communication is submitted in reply to the Notice mailed November 29, 2002 in connection with the above-identified application. A reply is due January 29, 2003. Therefore, this Communication is being timely filed.

In response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures mailed by the United States Patent and Trademark Office on November 29, 2002, applicant submits the following documents for filing in the above-referenced patent application:

1. A copy of the Notice Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures mailed on November 29, 2002;
2. Statement Under 37 C.F.R. § 1.821-1.825;
3. Diskette Containing Computer Readable Format of Sequence Listing;
4. Paper copy of the Sequence Listing; and

Applicants: Jay M. Short et al.
U.S. Serial No.: 10/029,221
Filed: December 21, 2001
Page 2

5. Return Postcard.

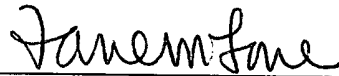
No fees are believed to be due in connection with this letter. However, please charge any additional costs or credit any overpayment to maintain the pendency of this application to our Deposit Account No. 08-0219.

If there are any questions, please call the undersigned at the telephone number indicated below.

Date: _____

1/9/03

Respectfully submitted,



Jane M. Love, Ph.D.
Registration No. 42,812
Attorney for Applicants

Hale and Dorr LLP
300 Park Avenue
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UNITED STATES
PATENT AND
TRADEMARK OFFICE

REC'D DEC 03 2002

Commissioner for Patents
Washington, DC 20231
www.uspto.gov

APPLICATION NUMBER	FILING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
10/029,221	12/21/2001	Jay M. Short	DIV-1460-21US (112766-199

CONFIRMATION NO. 4125

28089
HALE AND DORR LLP
300 PARK AVENUE
NEW YORK, NY 10022

FORMALITIES LETTER



OC000000009175999

Date Mailed: 11/29/2002

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS
CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE
DISCLOSURES**

Filing Date Granted

Applicant is given **TWO MONTHS FROM THE DATE OF THIS NOTICE** within which to file the items indicated below to avoid abandonment. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

- A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing." Applicant must provide a substitute computer readable form (CRF) copy of the "Sequence Listing" and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d).

For questions regarding compliance to these requirements, please contact:

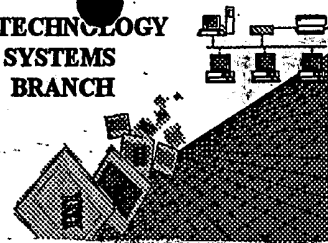
- For Rules Interpretation, call (703) 308-4216
- To Purchase PatentIn Software, call (703) 306-2600
- For PatentIn Software Program Help, call (703) 306-4119 or e-mail at patin21help@uspto.gov or patin3help@uspto.gov

*A copy of this notice **MUST** be returned with the reply.*


Customer Service Center

Initial Patent Examination Division (703) 308-1202

PART 1 - ATTORNEY/APPLICANT COPY



RAW SEQUENCE LISTING **ERROR REPORT**

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/029,221B
Source: OIPF
Date Processed by STIC: 11/6/02

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.

PATENTIN 2.1 e-mail help: patin21help@uspto.gov or phone 703-306-4119 (R. Wax)

PATENTIN 3.0 e-mail help: patin3help@uspto.gov or phone 703-306-4119 (R. Wax)

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE **CHECKER**
VERSION 3.1 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND
TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202
3. Hand Carry directly to:
U.S. Patent and Trademark Office, Technology Center 1600, Reception Area, 7th Floor, Examiner Name,
Sequence Information, Crystal Mall One, 1911 South Clark Street, Arlington, VA 22202
Or
U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two,
2011 South Clark Place, Arlington, VA 22202
4. Federal Express, United Parcel Service, or other delivery service to: U.S. Patent and Trademark Office,
Box Sequence, Room 1B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 01/29/2002



Does Not Comply
Corrected Diskette Needed

OIPE

Error on p. 3

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002
TIME: 14:55:15

Input Set : A:\112766-199.ST25.txt
Output Set: N:\CRF4\11062002\J029221B.raw

3 <110> APPLICANT: Short, Jay M.
4 Djavakhishvili, Tsotne David
5 Frey, Gerhard Johann
7 <120> TITLE OF INVENTION: Exonuclease-Mediated Nucleic Acid Reassembly in Directed
Evolution
9 <130> FILE REFERENCE: 112766.199
11 <140> CURRENT APPLICATION NUMBER: US 10/029,221B
C--> 12 <141> CURRENT FILING DATE: 2002-10-23
14 <150> PRIOR APPLICATION NUMBER: US 60/008,311
15 <151> PRIOR FILING DATE: 1995-12-07
17 <150> PRIOR APPLICATION NUMBER: US 60/008,316
18 <151> PRIOR FILING DATE: 1995-12-07
20 <160> NUMBER OF SEQ ID NOS: 12
22 <170> SOFTWARE: FastSEQ for Windows Version 4.0
24 <210> SEQ ID NO: 1
25 <211> LENGTH: 30
26 <212> TYPE: DNA
27 <213> ORGANISM: Artificial Sequence
29 <220> FEATURE:
30 <223> OTHER INFORMATION: defined sequence kernel

W--> 32 <221> NAME/KEY: misc_feature
33 <222> LOCATION: 1, 2, 4, 5, 7, 8, 10, 11, 13, 14, 16, 17, 19, 20, 22, 23,
34 25, 26, 28, 29
35 <223> OTHER INFORMATION: n = A,T,C or G
W--> 37 <400> 1
W--> 38 nnknnknnkn nknnknnknn knnknnknnk 30
40 <210> SEQ ID NO: 2
41 <211> LENGTH: 30
42 <212> TYPE: DNA
43 <213> ORGANISM: Artificial Sequence
45 <220> FEATURE:
46 <223> OTHER INFORMATION: defined sequence kernel
W--> 48 <221> NAME/KEY: misc_feature
49 <222> LOCATION: 1, 2, 4, 5, 7, 8, 10, 11, 13, 14, 16, 17, 19, 20, 22, 23,
50 25, 26, 28, 29
51 <223> OTHER INFORMATION: n = A,T,C or G
W--> 53 <400> 2
W--> 54 nnnnnnnnnnn nnnnnnnnnnn mnnnnnnnnnn 30
56 <210> SEQ ID NO: 3
57 <211> LENGTH: 5
58 <212> TYPE: PRT
59 <213> ORGANISM: Artificial Sequence
61 <220> FEATURE:
62 <223> OTHER INFORMATION: spacer peptide sequence of any number

RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002

TIME: 14:55:15

Input Set : A:\112766-199.ST25.txt

Output Set: N:\CRF4\11062002\J029221B.raw

64 <400> SEQUENCE: 3
65 Gly Gly Gly Gly Ser
66 1 5
69 <210> SEQ ID NO: 4
70 <211> LENGTH: 15
71 <212> TYPE: PRT
72 <213> ORGANISM: Artificial Sequence
74 <220> FEATURE:
75 <223> OTHER INFORMATION: linker peptide sequence
77 <400> SEQUENCE: 4
78 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
79 1 5 10 15
82 <210> SEQ ID NO: 5
83 <211> LENGTH: 10
84 <212> TYPE: DNA
85 <213> ORGANISM: Artificial Sequence
87 <220> FEATURE:
88 <223> OTHER INFORMATION: primer
90 <400> SEQUENCE: 5
91 aaggaggag 10
93 <210> SEQ ID NO: 6
94 <211> LENGTH: 24
95 <212> TYPE: DNA
96 <213> ORGANISM: Artificial Sequence
98 <220> FEATURE:
99 <223> OTHER INFORMATION: forward primer
W--> 101 <221> NAME/KEY: misc_feature
102 <222> LOCATION: 24
103 <223> OTHER INFORMATION: n = A,T,C or G from 10 to 100

W--> 105 <400> 6
W--> 106 ctagaagaga ggagaaaacc atgn 24
108 <210> SEQ ID NO: 7
109 <211> LENGTH: 22
110 <212> TYPE: DNA
111 <213> ORGANISM: Artificial Sequence
113 <220> FEATURE:
114 <223> OTHER INFORMATION: reverse primer
W--> 116 <221> NAME/KEY: misc_feature
117 <222> LOCATION: 22
118 <223> OTHER INFORMATION: n = A,T,C or G from 10 to 100
W--> 120 <400> 7
W--> 121 gatcaaaggc gcgcctgcag gn 22
123 <210> SEQ ID NO: 8
124 <211> LENGTH: 23
125 <212> TYPE: DNA
126 <213> ORGANISM: Artificial Sequence
128 <220> FEATURE:
129 <223> OTHER INFORMATION: forward primer
131 <400> SEQUENCE: 8

RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002

TIME: 14:55:15

Input Set : A:\112766-199.ST25.txt

Output Set: N:\CRF4\11062002\J029221B.raw

132 ctagaaggga ggagaaaacc atg 23
134 <210> SEQ ID NO: 9
135 <211> LENGTH: 21
136 <212> TYPE: DNA
137 <213> ORGANISM: Artificial Sequence
139 <220> FEATURE:
140 <223> OTHER INFORMATION: reverse primer
142 <400> SEQUENCE: 9
143 gatcaaaggc ggcctgcag g 21
145 <210> SEQ ID NO: 10
146 <211> LENGTH: 43
147 <212> TYPE: PRT
148 <213> ORGANISM: Artificial Sequence
150 <220> FEATURE:
151 <223> OTHER INFORMATION: primer
W--> 153 <221> NAME/KEY: VARIANT *also Xaa found at position 23*
154 <222> LOCATION: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16,
155 17, 18, 19, 20, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33,
156 34, 35, 36, 37, 38, 39, 40, 41, 42, 43
157 <223> OTHER INFORMATION: Xaa = Any Amino Acid
W--> 159 <221> VARIANT
160 <222> LOCATION: 23
161 <223> OTHER INFORMATION: Xaa = Gly or Thr
W--> 163 <400> 10
W--> 164 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
165 1 5 10 15
W--> 166 Xaa Xaa Xaa Xaa Asn Asn Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
167 20 25 30
W--> 168 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
169 35 40

172 <210> SEQ ID NO: 11
173 <211> LENGTH: 39
174 <212> TYPE: DNA
175 <213> ORGANISM: Artificial Sequence
177 <220> FEATURE:
178 <223> OTHER INFORMATION: forward primer
180 <400> SEQUENCE: 11
181 ctagaaggga ggagaattac atgaagcggc ttttagccc 39
183 <210> SEQ ID NO: 12
184 <211> LENGTH: 27
185 <212> TYPE: DNA
186 <213> ORGANISM: Artificial Sequence
188 <220> FEATURE:
189 <223> OTHER INFORMATION: reverse primer
191 <400> SEQUENCE: 12
192 agctaagggt caaggccgca cccgagg 27

RAW SEQUENCE LISTING ERROR SUMMARY
PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002
TIME: 14:55:16

Input Set : A:\112766-199.ST25.txt
Output Set: N:\CRF4\11062002\J029221B.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:1; N Pos. 1,2,4,5,7,8,10,11,13,14,16,17,19,20,22,23,25,26,28,29
Seq#:2; N Pos. 1,2,4,5,7,8,10,11,13,14,16,17,19,20,22,23,25,26,28,29
Seq#:6; N Pos. 24
Seq#:7; N Pos. 22
Seq#:10; Xaa Pos. 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,23,24
Seq#:10; Xaa Pos. 25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43

VERIFICATION SUMMARY

PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002

TIME: 14:55:16

Input Set : A:\112766-199.ST25.txt

Output Set: N:\CRF4\11062002\J029221B.raw

L:12 M:271 C: Current Filing Date differs, Replaced Current Filing Date
 L:32 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
 L:37 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
 L:38 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0
 L:48 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
 L:53 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
 L:54 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:0
 L:101 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
 L:105 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:6
 L:106 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:6 after pos.:0
 L:116 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
 L:120 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:7
 L:121 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:7 after pos.:0
 L:153 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
 L:159 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:10
 L:163 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:10
 L:164 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10 after pos.:0
 L:166 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10 after pos.:16
 L:168 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10 after pos.:32